EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	186	benzoyl adj cyanide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L2	960	(544/182).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L3	291	(558/388).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L4	349	(558/408).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:30
L5	1	jozsef.inv. and neu.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:31
L6	1	tibor.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L7	1	tibor.inv. and gizur.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L8	1	jozsef.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L9	1	ferenc.inv. and vegh.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L10	1	peter.inv. and kalvin.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34
L11	0	Gabor.inv. and Tarkanyl.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34

EAST Search History

L12	1	Gabor.inv. and Tarkanyi.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:36
L13	1	lamotrigine and 1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:37
L14	0	lamotrigine and (methane adj sulfonic adj acid)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:38
L15	83	lamotrigine and (sulfonic adj acid)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:38

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	186	benzoyl adj cyanide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L2	960	(544/182).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L3	291	(558/388).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L4	349	(558/408).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:30
L5	1	jozsef.inv. and neu.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:31
L6	1	tibor.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L7	1	tibor.inv. and gizur.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L8	1	jozsef.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L9	1	ferenc.inv. and vegh.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L10	1	peter.inv. and kalvin.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34
L11	0	Gabor.inv. and Tarkanyl.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34

EAST Search History

L12	1	Gabor.inv. and Tarkanyi.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:36
L13	1	lamotrigine and 1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:37
L14	0	lamotrigine and (methane adj sulfonic adj acid)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:38
L15	83	lamotrigine and (sulfonic adj acid)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:38

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	186	benzoyl adj cyanide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L2	960	(544/182).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L3	291	(558/388).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L4	349	(558/408).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:30
L5	1	jozsef.inv. and neu.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:31
L6	1	tibor.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L7	1	tibor.inv. and gizur.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L8	1	jozsef.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L9	1	ferenc.inv. and vegh.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L10	1	peter.inv. and kalvin.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34
L11	0	Gabor.inv. and Tarkanyi.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34

EAST Search History

L12	1	Gabor.inv. and Tarkanyi.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	186	benzoyl adj cyanide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L2	960	(544/182).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L3	291	(558/388).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:27
L4	349	(558/408).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:30
L5	1	jozsef.inv. and neu.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:31
L6	1	tibor.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L7	1	tibor.inv. and gizur.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:32
L8	1	jozsef.inv. and torley.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L9	1	ferenc.inv. and vegh.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:33
L10	1	peter.inv. and kalvin.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34
L11	0	Gabor.inv. and Tarkanyi.inv. and 2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/09/22 09:34

10/528,379

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NEWS 11	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
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NEWS 13	JUl 14	FSTA enhanced with Japanese patents
NEWS 14	JUl 19	Coverage of Research Disclosure reinstated in DWPI
NEWS 15	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 16	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 17	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 19	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation

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FILE LAST UPDATED: 21 Sep 2006  (20060921/ED)

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=> s lamotrigine/cn
   REG1stRY INITIATED
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L2        1143 L1

=> s l2 and (methane(l)sulfonic(ll)acid
MISSING OPERATOR 'SULFONIC(LL'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s methane(l)sulfonic(l)acid
        171134 METHANE
         77390 SULFONIC
       4215701 ACID
L3         712 METHANE(L)SULFONIC(L)ACID

=> s l2 and l3
L4           0 L2 AND L3

=> s l2 and process
       2310765 PROCESS
L5          53 L2 AND PROCESS
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=> s l5 and l3
L6            0 L5 AND L3

=> s l5 and magnesium(l)oxide
        464377 MAGNESIUM
       1688305 OXIDE
         86319 MAGNESIUM(L)OXIDE
L7            1 L5 AND MAGNESIUM(L)OXIDE

=> d l5 1-53 bib abs

L5   ANSWER 1 OF 53  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2006:149768  CAPLUS
DN   144:232798
TI   Preparation of nitroxyalkyl derivatives of phenol for treating
     inflammatory, cardiovascular and peripheral vascular diseases
IN   Ongini, Ennio; Impagnatiello, Francesco
PA   Nicox S.A., Fr.
SO   PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
PI   WO 2006015930         A1    20060216    WO 2005-EP53500          20050720
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2004-599857P       P     20040810
OS   MARPAT 144:232798
GI
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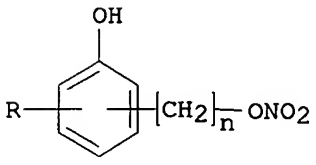


I

AB The title compds. I [n = 1-20; R = H, halo, a linear or branched (C1-C10)alkoxy, OH, CF3, NHR' (wherein R' = H or a linear or branched (C1-C10)alkyl); or a salt thereof], useful for treating inflammatory disease states or disorders, cardiovascular and/or peripheral vascular diseases, were prepared E.g., a benzenemethanol, 3-hydroxy-α-nitrate (II) was prepared from com. available 3-[(hydroxy)methyl]phenol using 2-step process. Effects of II on inflammatory markers were tested. For example, the compound II applied alone or in combination with ASA inhibited LPS/INFγ-induced nitrites accumulation with similar potency as that

estimated for NCX 4016 (EC50 = 58 μM and 57 μM, resp. for compound II alone and in combination with ASA). The pharmaceutical compns. comprising the compound II alone or in combination with other therapeutic agents are disclosed.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:149494 CAPLUS
DN 144:205795
TI Preventing pathological increases in the rate of nerve cell suicide in immature nervous systems
IN Olney, John W.
PA Olney, John, W., USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006017524	A2	20060216	WO 2005-US27460	20050802
WO 2006017524	A3	20060831		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-598390P P 20040802

AB Methods and compds. are disclosed for reducing brain damage in fetuses, neonates, and young infants, caused by surgical anesthetics. During critical periods of synapse formation and network development in the brain, CNS neurons that do not appear to be keeping pace with certain synchronized development and connection processes are regarded as surplus, and are destroyed by a programmed cell suicide process called apoptosis. As a result, if surgical anesthetics block neuronal responses and activities that normally would indicate that a certain CNS neuron is indeed active and involved in a network and should be preserved, such anesthesia can induce apoptotic death, in the unresponsive anesthetized neurons. That process, which can cause permanent brain damage, can be minimized by manipulating certain signaling pathways that affect the balance between apoptosis-promoting proteins (e.g., Bax and Bak) and apoptosis-blocking proteins (e.g., Bcl-2 and Bcl-xL). Agents that have been tested and shown to reduce anesthesia-induced brain damage in neonatal animals include xenon (which promotes ERK MAPKinase activity), and muscarinic cholinergic agonists (which can promote ERK MAPKinase, PKA, PKC, and/or PI3K/AKT activity). Other candidate agents with similar activities include lithium, beta-1 adrenergic antagonists, and beta-2 adrenergic agonists. Such agents must intervene in the "upstream" part of the apoptosis cascade, before mitochondrial membranes become permeable and begin to release "cytochrome c" messenger mols.

L5 ANSWER 3 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:100738 CAPLUS

DN 144:198849
TI Novel dosage form comprising modified-release and immediate-release active ingredients
IN Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar
PA India
SO U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2006024365	A1	20060202	US 2005-134633	20050519
	IN 193042	A	20040626	IN 2002-MU697	20020805
	US 2004096499	A1	20040520	US 2003-630446	20030729
PRAI	IN 2002-MU697	A	20020805		
	IN 2002-MU699	A	20020805		
	IN 2003-MU80	A	20030122		
	IN 2003-MU82	A	20030122		
	US 2003-630446	A2	20030729		

AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.

L5 ANSWER 4 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1325072 CAPLUS
DN 144:342887
TI Properties of antiepileptic drugs in the treatment of idiopathic generalized epilepsies
AU Patsalos, Philip N.
CS Institute of Neurology, London, UK
SO Epilepsia (2005), 46(Suppl. 9), 140-148
CODEN: EPILAK; ISSN: 0013-9580
PB Blackwell Publishing, Inc.
DT Journal; General Review
LA English
AB A review. Although valproate is considered to be the drug of first choice for the treatment of idiopathic generalized epilepsies (IGEs), other antiepileptic drugs (AEDs), both old (ethosuximide, clobazam, and clonazepam) and new (lamotrigine, levetiracetam, topiramate, and zonisamide) are also available. These AEDs do not appear to have a common mechanism of action in that both inhibitory gamma-aminobutyric acid (GABA; e.g., clobazam, clonazepam, and valproate) and excitatory glutamate (e.g., lamotrigine and topiramate) mechanisms are involved. Ethosuximide primarily acts by blocking T-type voltage-gated calcium channels in thalamic neurons while topiramate and zonisamide have multiple mechanisms of action. In contrast, levetiracetam is unique in that it may act via a specific binding site in the brain. In terms of their pharmacokinetic characteristics, all eight AEDs are rapidly absorbed after oral ingestion with peak blood concentration being achieved within 1-4 h. Bioavailability is 100% with the exception clonazepam (90%) and topiramate (81-95%). Plasma protein binding is variable with valproate (90%), clobazam (85%) and clonazepam (86%) showing substantial binding, lamotrigine (55%) and zonisamide (50%) intermediate binding, and levetiracetam (0%), ethosuximide (0%) and topiramate (10%) being minimally bound. However,

the binding by zonisamide is complicated by its binding to erythrocytes as well as albumin. All AEDs, with the exception of lamotrigine and levetiracetam, undergo elimination as a result of extensive metabolism by hepatic cytochrome P 450 enzymes, which are highly amenable to induction and inhibition by other drugs and therefore susceptible to pharmacokinetic interactions. Lamotrigine metabolism is via hepatic glucuronidation, a process that is also susceptible to induction and inhibition by concurrent drugs. Levetiracetam is minimally metabolized (by hydrolysis in blood), is excreted predominantly unchanged in urine, and to date has not been associated with any clin. significant pharmacokinetic interactions. Using a semiquant. pharmacokinetic rating system, based on 16 pharmacokinetic characteristics, a direct comparison between AEDs is possible. Thus valproic acid, regarded as the drag of first choice in the treatment of IGEs, rates lowest with respect to favorable pharmacokinetic characteristics, mostly because of its nonlinear pharmacokinetics, extensive hepatic metabolism, and its high propensity to interact both with other AEDs and non-AEDs. Levetiracetam rates highest with topiramate in second place.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1226325 CAPLUS
DN 144:114081
TI Predicting MDCK cell permeation coefficients of organic molecules using membrane-interaction QSAR analysis
AU Chen, Li-li; Yao, Jia; Yang, Jian-bo; Yang, Jie
CS State Key Laboratory of Pharmaceutical Biotechnology, College of Life Sciences, Nanjing University, Nanjing, 210093, Peop. Rep. China
SO Acta Pharmacologica Sinica (2005), 26(11), 1322-1333
CODEN: APSCG5; ISSN: 1671-4083
PB Blackwell Publishing Asia Pty Ltd.
DT Journal
LA English
AB Aim: To use membrane-interaction quant. structure-activity relationship anal. (MI-QSAR) to develop predictive models of partitioning of organic compds. in gastrointestinal cells. A training set of 22 structurally diverse compds., whose apparent permeability across cellular membranes of Madin-Darby canine kidney (MDCK) cells were measured, were used to construct MI-QSAR models. Mol. dynamic simulations were used to determine the explicit interaction of each test compound (solute) with a dimyristoyl-phosphatidyl-choline monolayer membrane model. An addnl. set of intramol. solute descriptors were computed and considered in the trial pool of descriptors for building MI-QSAR models. The QSAR models were optimized using multidimensional linear regression fitting and the stepwise method. A test set of 8 compds. were evaluated using the MI-QSAR models as part of a validation process. MI-QSAR models of the gastrointestinal absorption process were constructed. The descriptors found in the best MI-QSAR models are as follows: (1) ClogP (the logarithm of the 1-octanol/water partition coefficient); (2) EHOMO (the HOMO energy); (3) Es (stretch energy); (4) PMY (the principal moment of inertia Y, the inertia along the y axis in the rectangular coordinates; (5) Ct (total connectivity); and 6) Enb (the energy of interactions between all of the non-bonded atoms). The most important descriptor in the models is ClogP. Permeability is not only determined by the properties of drug mols., but is also very much influenced by the mol.-membrane interaction process.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:1015842 CAPLUS
DN 144:141916
TI Stability of Salivary Concentrations of the Newer Antiepileptic Drugs in the Postal System
AU Jones, Mikael D.; Ryan, Melody; Miles, Michael V.; Tang, Peter H.; Fakhoury, Toufic A.; De Grauw, Ton J.; Baumann, Robert J.
CS University of Kentucky Chandler Medical Center, Lexington, KY, 40536-0082, USA
SO Therapeutic Drug Monitoring (2005), 27(5), 576-579
CODEN: TDMODV; ISSN: 0163-4356
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Saliva antiepileptic drug (AED) concns. strongly correlate with serum concns. Saliva collection is painless and noninvasive, and untrained personnel can easily be taught the collection process. Remote patients could mail saliva samples to a laboratory for monitoring, and samples could be obtained in the immediate postictal state to provide a "real-time" concentration The objectives of this study were to assess the stability of saliva lamotrigine (LMT), levetiracetam (LEV), oxcarbazepine (OXC), topiramate (TPM), and zonisamide (ZNS) concns. sent through the United States Postal Service (USPS) and to quantify the amount of time needed for patients and the USPS to return samples to clinic. Saliva samples were obtained from patients currently taking 1 of the targeted AEDs. Samples were split into 2 storage vials. One sample was sealed in an addressed envelope, which the patient mailed from home, whereas the other sample was frozen immediately. Postmark date and day returned were collected for mailed samples. Saliva concns. were determined using HPLC. Wilcoxon rank sum tests were used to compare the immediately-frozen and mailed sample means. Correlations were determined by the Spearman test. Thirty-seven patients were enrolled in the study. The median time between collection and postmark was 1 day (range 0-6 days); and between collection and receipt was 4 days (range 1-160 days). The mean concns. for mailed and immediately frozen samples were similar for each AED ($P > 0.15$). Spearman rank order correlations between mailed and immediately frozen aliquots were strong (LMT rs = 1, LEV rs = 1, OXC rs = 0.964, TPM rs = 0.90, and ZNS rs = 1). Saliva samples mailed by patients maintain stability and can be returned in a reasonable length of time. Further studies are needed to assess patient/caretaker capability of obtaining an adequate sample.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:799772 CAPLUS
DN 143:199571
TI Transbuccal delivery of lamotrigine across porcine buccal mucosa: In vitro determination of routes of buccal transport
AU Mashru, Rajashree; Sutariya, Vijay; Sankalia, Mayur; Sankalia, Jolly
CS Pharmacy Department, Faculty of Technology and Engineering, The M. S. University of Baroda, Vadodara, India
SO Journal of Pharmacy & Pharmaceutical Sciences (2005), 8(1), 54-62
CODEN: JPPSFY; ISSN: 1482-1826
URL: http://www.ualberta.ca/~csps/JPPS8(1)/V.Sutariya/lamotrigine.pdf
PB Canadian Society for Pharmaceutical Sciences
DT Journal; (online computer file)
LA English
AB The aim was to determine the major routes of buccal transport of lamotrigine and to examine the effects of pH on drug permeation. Transbuccal permeation of lamotrigine across porcine buccal mucosa was studied by using in-line Franz type diffusion cell at 37°C. The permeability

of lamotrigine was determined at pH 4.0 to 9.0. The permeability of unionized (Pu) and ionized (Pi) species of drug were calculated by fitting the data to a math. model. Lamotrigine was quantified by using the HPLC method. The steady state flux increased linearly with increasing the donor concentration (r2 = 0.9639) at pH 7.4. The permeability coefficient and the partition coefficient of the drug increased with increasing the pH. The values of Pu and Pi were 0.7291 + 10-5 cm/s and 0.2500 + 10-5cm/s, resp. The observed permeability coeffs. and the permeability coeffs. calculated from math. model at various pH showed good linearity (r2 = 0.9267). The total permeability coefficient increased with increasing the fraction of unionized form of the drug. Lamotrigine permeated through buccal mucosa by a passive diffusion process. The partition coefficient and pH dependency of drug permeability indicated that lamotrigine was transported mainly via the transcellular route by a partition mechanism.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:611671 CAPLUS
DN 143:126805
TI Method of biochemical treatment of persistent pain by inhibiting biochemical mediators of inflammation
IN Omoigui, Osemwota Sota
PA USA
SO U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 224,743.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005152905	A1	20050714	US 2005-58371	20050216
	US 2004038874	A1	20040226	US 2002-224743	20020822
PRAI	US 2002-224743	A2	20020822		

AB The invention discloses a method for the biochem. treatment of persistent pain disorders by inhibiting the biochem. mediators of inflammation in a subject, comprising administering to the subject any one of several combinations of components that are inhibitors of biochem. mediators of inflammation. The process for biochem. treatment of persistent pain disorders is based on Sota Omoigui's Law, which states: 'The origin of all pain is inflammation and the inflammatory response'. Sota Omoigui's Law of Pain unifies all pain syndromes as sharing a common origin of inflammation and the inflammatory response. The various biochem. mediators of inflammation are present in differing amts. in all pain syndromes and are responsible for the pain experience. Classification and treatment of pain syndromes should depend on the complex inflammatory profile. A variety of mediators are generated by tissue injury and inflammation. These include substances produced by damaged tissue, substances of vascular origin as well as substances released by nerve fibers themselves, sympathetic fibers and various immune cells. Biochem. mediators of inflammation that are targeted for inhibition include but are not limited to: prostaglandin, nitric oxide, tumor necrosis factor α, interleukin 1α, interleukin 1β, interleukin 4, Interleukin 6, and interleukin 8, histamine and serotonin, substance P, matrix metalloproteinase, calcitonin gene-related peptide, vasoactive intestinal peptide, as well as the potent inflammatory mediator peptide proteins neurokinin A, bradykinin, kallidin and T-kinin.

L5 ANSWER 9 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:493490 CAPLUS
DN 143:32332
TI Water dispersible tablet
IN Gupta, Vinod Kumar; Vaya, Navin; Sougata, Pramanick
PA Torrent Pharmaceuticals Limited, India
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005051350	A2	20050609	WO 2004-IN312	20041007
WO 2005051350	A3	20050818		
WO 2005051350	B1	20050929		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI IN 2003-MU1128 A 20031028

AB This invention relates to a water-dispersible formulation of an active pharmaceutical ingredient or pharmaceutically acceptable salt hereof and one or more adjuvants without the use of swellable clay. More particularly, the invention comprises a dispersible formulation of anti-epileptic drug - lamotrigine. This invention further relates to a process for the preparation of said formulation.

L5 ANSWER 10 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:421792 CAPLUS
DN 142:430313
TI Process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (Lamotrigine) via reaction of 2,3-dichlorobenzoyl chloride with cuprous cyanide and then with aminoguanidine bicarbonate followed by cyclization.
IN Vyas, Sharad Kumar
PA Torrent Pharmaceuticals Ltd., India
SO Indian, 12 pp.
CODEN: INXXAP
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI IN 183150	A	19990925	IN 1998-CA2171	19981214
CA 2334937	AA	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 2000012924	A5	20000703	AU 2000-12924	19991207
	EP 1140872	A1	20011010	EP 1999-956293	19991207
	EP 1140872	B1	20030917		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 250041	E	20031015	AT 1999-956293	19991207
	RU 2231526	C2	20040627	RU 2001-115698	19991207
	US 6111101	A	20000829	US 1999-456501	19991208
PRAI	IN 1998-CA2171	A	19981214		
	WO 1999-IB1955	W	19991207		

OS CASREACT 142:430313

AB Lamotrigine was prepared by reaction of 2,3-dichlorobenzoyl chloride with CuCN (1:1-2 molar ratio) in MeCN and a cosolvent to produce dichlorobenzoyl cyanide, reaction of the latter with aminoguanidine bicarbonate to produce the cyanoimine intermediate 2-[cyano(2,3-dichlorophenyl)methylene]hydrazinecarboximidamide, and cyclization of this in the presence of aqueous KOH at 80°-reflux.

L5 ANSWER 11 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:369133 CAPLUS

DN 142:435774

TI Compositions treatment of chronic inflammatory diseases

IN Shapiro, Howard K.

PA USA

SO U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 610,073, abandoned.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005090553	A1	20050428	US 2004-924945	20040824
PRAI	US 1992-906909	B2	19920630		
	US 1994-241603	B2	19940511		
	US 1997-814291	B2	19970310		
	US 2000-610073	B2	20000705		

OS MARPAT 142:435774

AB This invention defines novel compns. that can be used for clin. treatment of a class of chronic inflammatory diseases. Increased generation of carbonyl substances, aldehydes and ketones, occurs at sites of chronic inflammation and is common to the etiologies of all of the clin. disorders addressed herein. Such carbonyl substances are cytotoxic and addnl. serve to perpetuate and disseminate the inflammatory process. This invention defines use of compns., the orally administered required primary agents of which are primary amine derivs. of benzoic acid capable of reacting with the carbonyl substances. P-Aminobenzoic acid (or PABA) is an example of the required primary agent of the present invention. PABA has a small mol. weight, is water soluble, has a primary amine group which reacts with carbonyl-containing substances and is tolerated by the body in relatively high dosages for extended periods. The method of the present invention includes administration of a composition comprising: (1) an orally consumed primary agent; (2) a previously known medicament co-agent recognized as effective to treat a chronic inflammatory disease addressed herein administered to the mammalian subject via the oral route, other systemic routes of administration or via the topical route; and (3) optionally 1 or more addnl. orally consumed co-agent selected from the group consisting of antioxidants, vitamins, metabolites at risk of depletion, sulfhydryl co-agents, co-agents which may facilitate glutathione activity and nonabsorbable primary amine polymeric co-agents,

so as to produce an additive or synergistic physiol. effect of an anti-inflammatory nature.

L5 ANSWER 12 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:325504 CAPLUS
DN 142:379390
TI Pharmaceutical formulations comprising microparticles with improved dispersibility, suspendability or wettability
IN Chickering, Donald E.; Reese, Shaina; Narasimhan, Sridhar; Straub, Julie A.; Bernstein, Howard; Altreuter, David; Huang, Eric K.; Brito, Luis A.; Jain, Rajeev A.
PA USA
SO U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 324,550.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005079138	A1	20050414	US 2004-955261	20040930
	US 2004121003	A1	20040624	US 2002-324558	20021219
PRAI	US 2002-324558	A2	20021219		

AB Methods are provided for making a dry powder blend pharmaceutical formulation, comprising the steps of: (a) providing microparticles which comprise a pharmaceutical agent; (b) blending the microparticles with at least one excipient in the form of particles to form a powder blend; and (c) jet milling the powder blend to form a dry powder blend pharmaceutical formulation having improved dispersibility, suspendability, or wettability as compared to the microparticles of step (a) or the powder blend of step (b). The method can further include dispersing the dry powder blend pharmaceutical formulation in a liquid pharmaceutically acceptable vehicle to make an formulation suitable for injection. Alternatively, the method can further include processing the dry powder blend pharmaceutical formulation into a solid oral dosage form. In one embodiment, the microparticles of step (a) are formed by a solvent precipitation or crystallization process. PLGA microspheres containing mannitol and Tween 80 having number average particle size of 1.96 μm, and volume average particle size of 4.04 μm were prepared The jet milling provided significant particle deagglomeration.

L5 ANSWER 13 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:318166 CAPLUS
DN 143:52909
TI Prediction of intestinal epithelial transport of drug in (Caco-2) cell culture from molecular structure using in silico approaches during early drug discovery
AU Ponce, Yovani Marrero; Perez, Miguel A. Cabrera; Zaldivar, Vicente Romero; Sanz, Marival Bermejo; Mota, Dany Siverio; Torrens, Francisco
CS Department of Pharmacy, Faculty of Chemical-Pharmacy, Central University of Las Villas, Villa Clara, 54830, Cuba
SO Internet Electronic Journal of Molecular Design (2005), 4(2), 124-150
CODEN: IEJMAT; ISSN: 1538-6414
URL: ftp://biochempress.com/iejmd_2005_4_0124.pdf
PB BioChem Press
DT Journal; (online computer file)
LA English
AB Motivation: The high interest in the prediction of the intestinal absorption for new chemical entities is generated by the increasing rate in the synthesis of compds. by combinatorial chemical and the extensive cost of

the traditional evaluation methods. Method: Novel mol. descriptors have been applied to estimate the intestinal epithelial transport of drug in Caco-2 cell culture. Total and local (atom and atom-type) quadratic indexes used in this study were calculated by TOMOCOMD-CARDD software. Linear Discriminant Anal. (LDA) was used to obtain a quant. model that discriminates the high absorption compds. (P ≥ 8+10-6 cm/s) from those with moderate-poor absorption (P < 8+10-6 cm/s). A data set of 134 diverse structure drugs and two series of drugs-like compds. (12 compds.) were used as training and test set, resp. In addition, Multiple Linear Regression (MLR) has been carried out to derive QSPerR models. All statistical analyses were performed with the STATISTICA software package. Results: The obtained LDA model classified correctly 81.13% of compds. with moderate-poor absorption properties and the 96.30% of compds. with high absorption, showing a global good classification of 90.30% in the training set. The model showed a high Matthews' correlation coefficient (MCC = 0.80). Internal and external validation processes to demonstrate the robustness and predictive power of the obtained model were carried out. In this sense, the model classified correctly 87.31% (MCC = 0.73) in the leave-one-out cross-validation procedure. The discriminant model was also assessed by a 10 fold full cross-validation (removing approx. 13 compds. in each cycle, 85.82% of good classification), yielding a MCC of 0.70. Also this model shown an 87.5, 85.6, 84.7, 85.0, 85.3, 83.5, 84.1, 86.2, 85.9 and 85.9% of global good classification when n varied from 2 to 11 in the leave-n-out cross validation procedure. The model was stabilized around 85.9% when n was > 9. In addition, a data set of 7 HIV protease inhibitors (4 linear peptidomimetic and 3 new cyclic urea) and 5 new 6 fluoroquinolones derivs. was used as external test set. The LDA-QSPerR model achieved a MCC of 0.71 (83.33% correct prediction) in this study. This approach permits us to obtain a good explanation of the experiment based on the mol. structural features, evidencing the main role of H-bonding and size properties in permeability process. Finally, the model developed was used in the virtual screening of 241 drugs with the percentage of human intestinal absorption (Abs %) values reported. A relationship between the predicted permeability coeffs. in Caco-2 and the Abs % (145 compds. with good data quality) was established, with a percentage of good relation greater than 82 %. A comparison with results derived from other three theor. studies shown a quite satisfactory behavior of the present method. Conclusions: All these results shown that total and local (atom and atom-type) quadratic indexes can successfully predict intestinal permeability and suggest that the proposed methodol. will be a good tool for studying the oral absorption of drug candidates during the drug development process.

RE.CNT 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:216629 CAPLUS
DN 142:285200
TI Nanoparticles for drug delivery
IN Turos, Edward; Shim, Jeung-Yeop
PA University of South Florida, USA
SO PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005020933	A2	20050310	WO 2004-US28995	20040902
	WO 2005020933	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-499904P P 20030902
US 2003-500750P P 20030904
US 2004-568746P P 20040506

AB This invention relates to a unique process for the preparation of polymeric nanoparticles with target mols. bonded to the surface of the particles and having sizes of up to 1000 nm, preferably 1-400 nm, more preferably 1-200 nm, that are dispersed homogeneously in aqueous solution To accomplish the above objective, the polymeric nanoparticles of the subject invention are prepared using a novel technique of microemulsion polymerization The resulting aqueous solution of polymeric nanoparticles is comprised of about 1-100 parts per weight of water or buffer, about 1-80 parts per weight of polymeric nanoparticles, which the bioactive mols. are conjugated, about 0.001-10 parts per weight of emulsifier, and about 0.00001-5 parts per weight of radical initiator based on the weight of the solution In the method of this invention, the target drug/target substance is covalently bonded to the polymeric nanoparticles to secure them from outer intervention in vivo or cell culture in vitro until they are exposed at the target site within the cell. Nanoparticles of ethylacrylate-N-methylthiolated 3-lactam copolymer were prepared by a radical polymerization using potassium persulfate as the initiator and the sodium salt of dodecyl sulfate as the surfactant. The particle size was 40-80 nm. The antibacterial activity of the nanoparticles is shown.

L5 ANSWER 15 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:881202 CAPLUS
DN 142:48479
TI A topological sub-structural approach for predicting human intestinal absorption of drugs
AU Perez, Miguel Angel Cabrera; Sanz, Marival Bermejo; Torres, Liliana Ramos; Avalos, Ricardo Grau; Gonzalez, Maykel Perez; Diaz, Humberto Gonzalez
CS Center of Chemical Bioactive, Department of Drug Design, Central University of Las Villas, Las Villas, Santa Clara, 54830, Cuba
SO European Journal of Medicinal Chemistry (2004), 39(11), 905-916
CODEN: EJMCA5; ISSN: 0223-5234
PB Elsevier Ltd.
DT Journal
LA English
AB The human intestinal absorption (HIA) of drugs was studied using a topol. sub-structural approach (TOPS-MODE). The drugs were divided into three classes according to reported cutoff values for HIA. "Poor" absorption was defined as HIA ≤30%, "high" absorption as HIA ≥80%, whereas "moderate" absorption was defined between these two values (30% < HIA < 79%). Two linear discriminant analyses were carried out on a training set of 82 compds. The percentages of correct classification, for both models, were 89.02%. The predictive power of the models were validated by three test: a leave-one-out cross validation procedure (88.9% and 87.9%), an external prediction set of 127 drugs (92.9% and 80.31%) and a test set of 109 oral drugs with bioavailability values reported (93.58% and 91.84%). Finally, pos. and neg. sub-structural contributions to the

HIA were identified and their possibilities in the lead generation and optimization process were evaluated.
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:799572 CAPLUS
DN 141:282838
TI Novel crystalline forms of lamotrigine
IN Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari; Subash, Chander Reddy Kesireddy
PA Hetero Drugs Limited, India
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004083191	A1	20040930	WO 2003-IN57	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003217437	A1	20041011	AU 2003-217437	20030317
US 2005119265	A1	20050602	US 2003-508099	20030317
EP 1603889	A1	20051214	EP 2003-712623	20030317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI WO 2003-IN57	A	20030317		

AB The present invention relates to novel crystalline forms of lamotrigine, to processes for their preparation and pharmaceutical compns. containing them. A process for preparation of crystalline forms of lamotrigine comprises steps of (i) dissolving lamotrigine in a solvent, (ii) maintaining the solvent at certain temperature for certain time, and (iii) filtering the crystal form solid. For example, 10 g of lamotrigine was added to 100 mL of dioxane, maintained at 50° to 55° for 60 min, cooled to 25°
and maintained at this temperature for 2 h. The solid was separated by filtration
to give 8.5 g of Form II lamotrigine.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:799438 CAPLUS
DN 141:282833
TI Stable lamotrigine pharmaceutical compositions
IN Mehta, Kamal; Mathur, Rajeev Shanker; Sethi, Sanjeev; Malik, Rajiv; Sinha, Suhani
PA Ranbaxy Laboratories Limited, India
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004082587	A2	20040930	WO 2004-IB820	20040319
	WO 2004082587	A3	20041202		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1608342	A2	20051228	EP 2004-721960	20040319
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRAI	IN 2003-DE355	A	20030321		
	WO 2004-IB820	W	20040319		

AB The present invention relates to a stable pharmaceutical composition of lamotrigine and pharmaceutically acceptable acid addition salts thereof. The invention also relates to a process for the preparation of such a composition The pharmaceutical composition includes: 0.1-50 lamotrigine or acid addition salt thereof, 15.5-70% microcryst. cellulose, 0.1-14.5% sodium starch glycolate, and 0.1-4.5% polyvinylpyrrolidone.

L5 ANSWER 18 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:780544 CAPLUS
DN 141:301421
TI Improved bioavailability and improved delivery of alkaline drugs
IN Yu, Ruey J.; Van Scott, Eugene J.
PA USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004080468	A1	20040923	WO 2004-US6699	20040305
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004214215	A1	20041028	US 2004-792273	20040304
	AU 2004220597	A1	20040923	AU 2004-220597	20040305
	CA 2517782	AA	20040923	CA 2004-2517782	20040305
	EP 1601366	A1	20051207	EP 2004-717955	20040305
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRAI	US 2003-452557P	P	20030307		
	US 2004-792273	A	20040304		

WO 2004-US6699 A 20040305
OS MARPAT 141:301421
AB Embodiments of the invention relate to a composition, a process of making the composition, and to the use of the composition The compns. include a mol. complex formed between an alkaline pharmaceutical and at least one selected from a hydroxyacid, a polyhydroxy acid, a related acid, a lactone, or combinations thereof. The compns. provide improved bioavailability and improved delivery of the drug into the cutaneous tissues. For example, diphenhydramine hydrochloride 29 g (0.1 mol) was dissolved in water (50 mL) and 5N sodium hydroxide (20 mL) was slowly added to generate diphenhydramine as a free base as shown by the formation of oily ppts. and the change from pH 5.5 to 9.4. Gluconolactone 18 g (0.1 mol) was added to form a mol. complex between the diphenhydramine free base and gluconic acid/gluconolactone as shown by the disappearance of the oily ppts. and the change from pH 9.4 to 7.4. The solution thus obtained contained 0.1 mol diphenhydramine in mol. complex with 0.1 mol gluconic acid/gluconolactone. This concentrated stock solution was used for various forms of topical formulations including oil-in-water creams, lotions, gels and solns.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:678666 CAPLUS
DN 141:325158
TI QSAR Models for the Prediction of Binding Affinities to Human Serum Albumin Using the Heuristic Method and a Support Vector Machine
AU Xue, C. X.; Zhang, R. S.; Liu, H. X.; Yao, X. J.; Liu, M. C.; Hu, Z. D.; Fan, B. T.
CS Department of Chemistry, Lanzhou University, Lanzhou, 730000, Peop. Rep. China
SO Journal of Chemical Information and Computer Sciences (2004), 44(5), 1693-1700
CODEN: JCISD8; ISSN: 0095-2338
PB American Chemical Society
DT Journal
LA English
AB The binding affinities to human serum albumin for 94 diverse drugs and drug-like compds. were modeled with the descriptors calculated from the mol. structure alone using a quant. structure-activity relationship (QSAR) technique. The heuristic method (HM) and support vector machine (SVM) were utilized to construct the linear and nonlinear prediction models, leading to a good correlation coefficient (R2) of 0.86 and 0.94 and root-mean-square errors (rms) of 0.212 and 0.134 albumin drug binding affinity units, resp. Furthermore, the models were evaluated by a 10 compound external test set, yielding R2 of 0.71 and 0.89 and rms error of 0.430 and 0.222. The specific information described by the heuristic linear model could give some insights into the factors that are likely to govern the binding affinity of the compds. and be used as an aid to the drug design process; however, the prediction results of the nonlinear SVM model seem to be better than that of the HM.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:640398 CAPLUS
DN 142:49039
TI Inhibitory effect of lamotrigine on A-type potassium current in hippocampal neuron-derived H19-7 cells

AU Huang, Chin-Wei; Huang, Chao-Ching; Liu, Yen-Chin; Wu, Sheng-Nan
CS Department of Neurology, Institute of Clinical Medicine, National Cheng-Kung University Medical Center, Tainan, Taiwan
SO Epilepsia (2004), 45(7), 729-736
CODEN: EPILAK; ISSN: 0013-9580
PB Blackwell Publishing, Inc.
DT Journal
LA English
AB Purpose: We investigated the effects of lamotrigine (LTG) on the rapidly inactivating A-type K+ Current (IA) in embryonal hippocampal neurons. Methods: The whole-cell configuration of the patch-clamp technique was applied to investigate the ion currents in cultured hippocampal neuron-derived H19-7 cells in the presence of LTG. Effects of various related compds. on IA in H19-7 cells were compared. Results: LTG (30 μM-3 mM) caused a reversible reduction in the amplitude of IA. The median inhibitory concentration (IC50) value required for the inhibition of IA by LTG was 160 μM. 4-Aminopyridine (1 mM), quinidine (30 μM), and capsaicin (30 μM) were effective in suppressing the amplitude of IA, whereas tetraethylammonium chloride (1 mM) and gabapentin (100 μM) had no effect on it. The time course for the inactivation of IA was changed to the biexponential process during cell exposure to LTG (100 μM). LTG (300 μM) could shift the steady-state inactivation of IA to a more neg. membrane potential by approx. -10 mV, although it had no effect on the slope of the inactivation curve. Moreover, LTG (100 μM) produced a significant prolongation in the recovery of IA inactivation. Therefore in addition to the inhibition of voltage-dependent Na+ channels, LTG could interact with the A-type K+ channels to suppress the amplitude of IA. The blockade of IA by LTG does not simply reduce current magnitude, but alters current kinetics, suggesting a state-dependent blockade. LTG might have a higher affinity to the inactivated state than to the resting state of the IA channel. Conclusions: This study suggests that in hippocampal neurons, during exposure to LTG, the LTG-mediated inhibition of these K+ channels could be one of the ionic mechanisms underlying the increased neuronal excitability.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:633439 CAPLUS
DN 141:167771
TI Tetracycline compounds having target therapeutic activities
IN Levy, Stuart B.; Draper, Michael; Nelson, Mark L.; Jones, Graham
PA Paratek Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 277 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004064728	A2	20040805	WO 2004-US1036	20040116
	WO 2004064728	A3	20041216		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	US 2006194773	A1	20060831	US 2004-996119	20041122
PRAI	US 2003-441141P	P	20030116		
	US 2001-305546P	P	20010713		
	US 2002-395741P	P	20020712		
	US 2002-196010	A2	20020715		

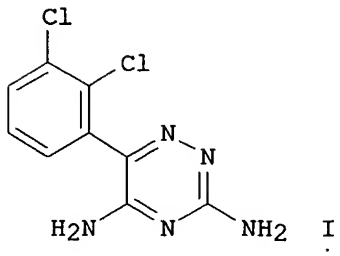
US 2004-759484 B1 20040116
OS MARPAT 141:167771
AB Methods and compds. for treating diseases, e.g. inflammation process-associated states, with tetracycline compds. having a target therapeutic activity are described. Preparation of selected tetracycline compds. is described.

L5 ANSWER 22 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:421470 CAPLUS
DN 141:7119
TI Preparation of crystalline lamotrigine and its monohydrate
IN Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundia; Bokka, Ravisankar
PA Jubilant Organosys Limited, India
SO Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2395483	A1	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2003-15608 A 20030703
OS CASREACT 141:7119
GI



I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent,
at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure

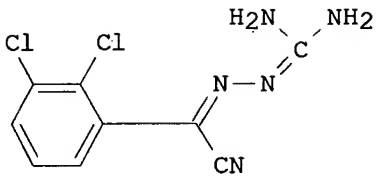
lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

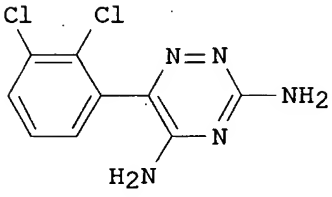
L5 ANSWER 23 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:390214 CAPLUS
DN 140:391299
TI Process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
IN Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi
PA Laboratorios Vita, S.A., Spain
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004039767	A1	20040513	WO 2003-IB4763	20031027
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	ES 2209639	A1	20040616	ES 2002-2502	20021031
	ES 2209639	B1	20050801		
	AU 2003272019	A1	20040525	AU 2003-272019	20031027
	EP 1556341	A1	20050727	EP 2003-753860	20031027
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2006052625	A1	20060309	US 2005-532397	20050422
	NO 2005002574	A	20050527	NO 2005-2574	20050527
PRAI	ES 2002-2502	A	20021031		
	WO 2003-IB4763	W	20031027		

OS CASREACT 140:391299
GI



I



II

AB A method for preparing the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an aliph alc. (e.g., ethanol) or alc.-water mixture

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:267313 CAPLUS
DN 140:303705
TI Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate
IN Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor
PA Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004026845	A1	20040401	WO 2003-HU72	20030918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2498761	AA	20040401	CA 2003-2498761	20030918
	AU 2003267676	A1	20040408	AU 2003-267676	20030918
	EP 1539720	A1	20050615	EP 2003-748368	20030918
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2006178511	A1	20060810	US 2005-528379	20051129
PRAI	HU 2002-3114	A	20020920		
	WO 2003-HU72	W	20030918		

OS CASREACT 140:303705

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB High-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I; i.e., lamotrigine) is prepared by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of methanesulfonic acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:252201 CAPLUS

DN 140:229472

TI Method using dopamine activity-modulating anticonvulsants for treatment of disorders of personal attachment and deficient social interaction

IN Daniel, David Gordon

PA USA

SO U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004058997	A1	20040325	US 2002-252716	20020924
PRAI US 2002-252716		20020924		

AB The invention provides a process for treatment of central nervous system disorders characterized by interpersonal discomfort and awkwardness, diminished social approach and initiative, and paucity of interpersonal attachments and social interactions. Abnormal perceptions of interpersonal communication and peculiarities of social behavior commonly accompany these symptoms. Inhibited initiation of social behavior and personal attachment are cardinal symptoms of schizotypal personality disorder, schizoid personality disorder, paranoid personality disorder, avoidant personality disorder; pervasive developmental disorder, and Aspberger's syndrome. These symptoms may also in the form of clin. significant social introversion that does not meet the threshold for a formal psychiatric disorder by current diagnostic stds. such as DSM-IV. The treatment provides a process of symptomatic relief and stabilization of the course of these disorders. The methodol. of the invention uses administration of an anticonvulsant which modulates dopamine activity.

L5 ANSWER 26 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:213191 CAPLUS
DN 140:368485
TI Pharmacological characterization of acid-induced muscle allodynia in rats
AU Nielsen, Alexander Norup; Mathiesen, Claus; Blackburn-Munro, Gordon
CS NeuroSearch A/S, Department of Pharmacology, Ballerup, DK-2750, Den.
SO European Journal of Pharmacology (2004), 487(1-3), 93-103
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB Previous studies have shown that repeated injections of acidic saline, given into the lateral gastrocnemius muscle of rats, results in a bilateral reduction in withdrawal threshold to tactile stimulation of the hindpaws. We have now characterized this model of muscoskeletal pain pharmacol., by evaluating the antinociceptive effects of various analgesics after systemic administration. The μ-opioid receptor agonist morphine (3 and 6 mg/kg) produced a particularly prolonged antiallodynic effect. The glutamate receptor antagonists NS1209 and ketamine (6 and 15 mg/kg, resp.), the KCNQ K+ channel openers retigabine and flupirtine (10 and 20 mg/kg, resp.) and the Na+ channel blocker mexiletine (37.5 mg/kg) also significantly increased paw withdrawal threshold, although to a lesser degree than morphine. In contrast, the anticonvulsant lamotrigine (30 mg/kg), the cyclooxygenase-2 inhibitor carprofen (15 mg/kg) and the benzodiazepine diazepam (3 mg/kg) were ineffective. All antinociceptive effects were observed at nonataxic doses as determined by the rotarod test. These results suggest that in this model, muscle-mediated pain can be alleviated by various analgesics with differing mechanisms of action, and that once established ongoing inflammation does not appear to contribute to this process.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:120697 CAPLUS
DN 140:169663
TI Dosage form containing modified- and immediated-release portions
IN Vaya, Navin; Karan, Rajesh Singh; Nadkarni, Sunil Sadanand
PA Torrent Pharmaceuticals Limited, India; Guota Vinod, Kumar
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004012700	A2	20040212	WO 2003-IN262	20030801
	WO 2004012700	A3	20040401		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	IN 193042	A	20040626	IN 2002-MU697	20020805
	AU 2003274681	A1	20040223	AU 2003-274681	20030801

	EP 1528917	A2	20050511	EP 2003-758649	20030801
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003013424	A	20050614	BR 2003-13424	20030801
	US 2006153916	A1	20060713	US 2006-522989	20060201
PRAI	IN 2002-MU697	A	20020805		
	IN 2002-MU699	A	20020805		
	IN 2003-MU80	A	20030122		
	IN 2003-MU82	A	20030122		
	WO 2003-IN262	W	20030801		

AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. An inner portion contained pravastatin sodium, lactose monohydrate, starch, Mg stearate, Na starch glycolate and dye to make tablets. An outer portion contained niacin, Eudragit RSPO to form granules and they were coated with hydrogenated castor oil in acetone and mixed with Mg stearate. Tablets were prepared by compression such that the resultant tablets have an inner portion covered by the outer portion from all sides except the top surface that remains uncovered and the level of the inner portion and the outer portion is on the same surface.

L5 ANSWER 28 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:991477 CAPLUS
DN 140:31517
TI Controlled release formulation of lamotrigine
IN Nadkarni, Sunil Sadanand
PA Torrent Pharmaceuticals Limited, India
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003104192	A2	20031218	WO 2003-IN213	20030606
	WO 2003104192	A3	20040311		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004043996	A1	20040304	US 2003-452772	20030602
	CA 2488868	AA	20031218	CA 2003-2488868	20030606
	AU 2003267808	A1	20031222	AU 2003-267808	20030606
	BR 2003011701	A	20050308	BR 2003-11701	20030606
	EP 1513535	A2	20050316	EP 2003-748504	20030606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-386795P	P	20020607		
	WO 2003-IN213	W	20030606		

AB Rapidly disintegrating multiparticulate controlled-release formulations of lamotrigine having an improved pharmacokinetic profile and improved

patient compliance, and process of preparing the formulations are described. The formulations comprise pelleted cores covered with one or more different rate-controlling polymeric membrane(s). It provides better control of blood plasma levels than conventional tablet formulations that is administered once or more times a day. For example, granules (core particles, diameter of 0.15 to 0.30 mm) were prepared using a fluidized bed processor from 750 g of microcryst. cellulose and a bulk liquid containing lamotrigine 900.00 g, hydroxypropyl Me cellulose 545.45 g, and water 13.20 kg. The 1500 g of the drug granules (core particles) were spray coated with a rate-controlling coating membrane composition containing Eudragit RS PO 163.84 g, Eudragit RL PO 8.617 g, tri-Et citrate 34.5 g, talc 55.52 g, methylene chloride 997.5 g, and iso-Pr alc. 1671.25 g to obtain controlled-release particles. The controlled-release particles prepared were filled into capsules (50 mg/capsule) and showed better pharmacokinetic profile than the conventional tablets.

L5 ANSWER 29 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:982733 CAPLUS
DN 140:176945
TI Water-protein and ligand-protein interactions as determined by selective NMR relaxation studies
AU Rossi, Claudio; Martini, Silvia; Ricci, Maso; Picchi, Maria Pia; Bonechi, Claudia
CS Department of Chemical and Biosystem Sciences, University of Siena, Siena, 2-53100, Italy
SO Macromolecular Symposia (2003), 203(4th International Conference on Polymer-Solvent Complexes and Intercalates, 2002), 89-101
CODEN: MSYMEC; ISSN: 1022-1360
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
AB Water-macromols. and ligand-macromols. interactions were investigated considering the effects induced by the presence of a macromol. on both the water and the ligand NMR selective (R1SE) and non-selective (R1NS) spin-lattice relaxation rates. The results obtained from the solvent studies were used to describe the solvent dynamics at the macromol.-solvent interface. On the other hand, ligand R1SE and R1NS anal. allowed the definition of the "affinity index", [A]TL, an index related to the extent of the macromol.-ligand recognition process

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 30 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:507707 CAPLUS
DN 139:69292
TI Process for the preparation of lamotrigine and related 3,5-diamino-6-substituted-1,2,4-triazines via cyclization of cyanoiminoguanidines.
IN Guntoori, Bhaskar Reddy; Che, Daqing; Murthy, K. S. Keshava
PA Brantford Chemicals Inc., Can.
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

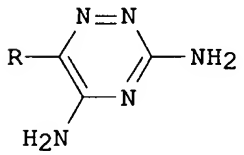
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6586593	B1	20030701	US 2002-46383	20020116
	CA 2366521	AA	20030624	CA 2001-2366521	20011224
	WO 2003078407	A1	20030925	WO 2002-CA1926	20021218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002367765	A1	20030929	AU 2002-367765		20021218
EP 1458692	A1	20040922	EP 2002-807048		20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
NZ 533734	A	20051223	NZ 2002-533734		20021218
PRAI CA 2001-2366521	A	20011224			
WO 2002-CA1926	W	20021218			

OS CASREACT 139:69292; MARPAT 139:69292

GI



I

AB Title compds. [I; R = (substituted) alkyl, aryl], were prepared by reaction of RCOCN with aminoguanidine in the presence of an organic sulfonic acid in an organic solvent under anhydrous conditions to give (HO)C(R)(CN)NHNC(NH2)2, dehydration of this to give NCC(R)[:NN:C(NH2)2], and cyclization of the latter. Thus, aminoguanidine hydrochloride in DMF was treated with MeSO3H and 2,3-dichlorobenzoyl chloride followed by stirring for 1 h, addition of SOCl2, and stirring for 1 h to give 39.2% iminoguanidine derivative The latter was refluxed with KOH in Me2CHOH to give 82% lamotrigine monohydrate.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 31 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:154224 CAPLUS
DN 138:193294
TI Expandable gastric retention device containing pharmaceutical compositions
IN Ayres, James W.
PA The State of Oregon Acting by and Through the State Board of Higher Education On Behalf of Oregon State University, USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003015745	A1	20030227	WO 2001-US46146	20011022

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,

US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2456976	AA	20030227	CA 2001-2456976	20011022
EP 1416914	A1	20040512	EP 2001-995328	20011022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001017123	A	20040928	BR 2001-17123	20011022
CN 1543337	A	20041103	CN 2001-823544	20011022
JP 2005501097	T2	20050113	JP 2003-520705	20011022
NO 2004000611	A	20040416	NO 2004-611	20040211
US 2004219186	A1	20041104	US 2004-778917	20040213
ZA 2004002066	A	20050509	ZA 2004-2066	20040315
PRAI US 2001-313078P	P	20010816		
WO 2001-US46146	W	20011022		

AB The present application concerns gastric retention devices formed from compns. comprising polymeric materials, such as polysaccharides, and optional addnl. materials including excipients, therapeutics, and diagnostics, that reside in the stomach for a controlled and prolonged period of time. Dry powders of xanthan gum and locust bean gum were mixed intimately were converted to dried films. The dried films were compressed with the help of specially made punches and dies. A series of dies with decreasingly narrow internal diams. were used. A punch pushes the film from one die into the next die, followed by pushing of the film by another punch into the next die. This process takes place in succession until a point is reached where the film is small enough to put into a desired capsule size.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 32 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:89558 CAPLUS
DN 139:270800
TI Effects of lamotrigine and levetiracetam on seizure development in a rat amygdala kindling model
AU Stratton, Sharon C.; Large, Charles H.; Cox, Brian; Davies, Gary; Hagan, Russell M.
CS Neurology and GI Centre of Excellence for Drug Discovery, New Frontiers Science Park, GlaxoSmithKline, Essex, CM19 5AW, UK
SO Epilepsy Research (2003), 53(1-2), 95-106
CODEN: EPIRE8; ISSN: 0920-1211
PB Elsevier Science B.V.
DT Journal
LA English
AB In kindling models of epilepsy, the period during which repeated stimulation evokes intensifying seizures is attributed to an underlying epileptogenic process, and the point at which class 5 kindled seizures occur is considered the established epileptic state. Previous studies have indicated that a separation can occur between drug effects on these two components. For example, carbamazepine and phenytoin inhibit kindled seizures but have no effect on seizure development, whereas levetiracetam inhibits both components. We have investigated the profile of lamotrigine in the amygdala kindling model, including levetiracetam for comparison. As expected, both treatments dose-dependently inhibited class 5 kindled seizures. In a sep. study, daily administration of either lamotrigine (20 mg kg-1 i.p.) or levetiracetam (50 mg kg-1 i.p.) demonstrated antiepileptogenic-like effects by blocking seizure development during the treatment period. Following cessation of drug treatment, further daily stimulation resulted in kindled seizure development, though there was a significant increase with both treatment

groups, relative to the control group, in the total number of stimulations required to produce classes 3 and 5 seizures. In addition, prior levetiracetam treatment appeared to delay or prevent the expected increase in after-discharge duration (ADD). These results suggest that lamotrigine, like levetiracetam, possesses the ability to counteract kindling acquisition, which differentiates it from other drugs with sodium channel blocking activity.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:57866 CAPLUS
DN 138:117673
TI Tetracycline compounds having target therapeutic activities
IN Levy, Stuart B.; Draper, Michael; Nelson, Mark L.; Jones, Graham
PA Paratek Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003005971	A2	20030123	WO 2002-US22451	20020715
	WO 2003005971	A3	20031127		
	WO 2003005971	C1	20040506		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002318238	A1	20030129	AU 2002-318238	20020715
	US 2004063674	A1	20040401	US 2002-196010	20020715
	EP 1408987	A2	20040421	EP 2002-748169	20020715
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2004537544	T2	20041216	JP 2003-511780	20020715
	US 2006194773	A1	20060831	US 2004-996119	20041122
PRAI	US 2001-305546P	P	20010713		
	US 2002-395741P	P	20020712		
	US 2002-196010	A2	20020715		
	WO 2002-US22451	W	20020715		
	US 2003-441141P	P	20030116		
	US 2004-759484	B1	20040116		

OS MARPAT 138:117673
AB Methods and compds. for treating a variety of diseases with tetracycline compds. having a target therapeutic activity are described, as is compound preparation

L5 ANSWER 34 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:846109 CAPLUS
DN 138:331608
TI Inhibition of Na+ current by imipramine and related compounds: different binding kinetics as an inactivation stabilizer and as an open channel blocker
AU Yang, Ya-Chin; Kuo, Chung-Chin

CS Department of Physiology, National Taiwan University College of Medicine, Taiwan
SO Molecular Pharmacology (2002), 62(5), 1228-1237
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Use-dependent block of Na+ channels plays an important role in the action of many medications, including the anticonvulsants phenytoin, carbamazepine, and lamotrigine. These anticonvulsants all slowly yet selectively bind to a common receptor site in inactivated but not resting Na+ channels, constituting the mol. basis of the use-dependent block. However, it remains unclear what channel gating process "makes" the receptor, where the receptor is located, and how the slow drug binding rate (to the inactivated channels) is contrived. Imipramine has a di-Ph structural motif almost identical to that in carbamazepine (a dibenzazepine tricyclic compound), as well as a tertiary amine chain similar to that in many prototypical local anesthetics, and has also been reported to inhibit Na+ channels in a use-dependent fashion. We found that imipramine selectively binds to the inactivated (dissociation constant .apprx.1.3 μM) rather than the resting Na+ channels (dissociation constant >130 μM). Moreover, imipramine rapidly blocks open Na+ channels, with a binding rate .apprx.70-fold faster than its binding to the inactivated channels. Similarly, carbamazepine and diphenhydramine are open Na+ channel blockers with faster binding rates to the open than to the inactivated channels. These findings indicate that the anticonvulsant receptor responsible for the use-dependent block of Na+ channels is located in or near the pore (most likely in the pore mouth) and is made suitable for drug binding during channel activation. The receptor, however, continually changes its conformation in the subsequent gating process, causing the slower drug binding rates to the inactivated Na+ channels.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:456939 CAPLUS
DN 138:214872
TI Time course of lamotrigine de-induction: impact of step-wise withdrawal of carbamazepine or phenytoin
AU Anderson, Gail D.; Gidal, Barry E.; Messenheimer, John A.; Gilliam, Frank G.
CS Department of Pharmacy, University of Washington, Seattle, WA, USA
SO Epilepsy Research (2002), 49(3), 211-217
CODEN: EPIRE8; ISSN: 0920-1211
PB Elsevier Science B.V.
DT Journal
LA English
AB Objective: The objective of the present anal. is to examine lamotrigine (LTG) pharmacokinetics both during polytherapy with enzyme inducing antiepileptic drugs and to evaluate the time course of de-induction following the step-wise withdrawal of enzyme inducers. Background: LTG pharmacokinetics can be significantly influenced by concomitant AEDs, and the addition of enzyme inducers can markedly increase LTG clearance, thereby reducing serum concns. A clin. relevant question is how will LTG clearance and resulting plasma concns. be altered during concomitant enzyme inducer withdrawal/conversion process. Design/Method: As part of a previously published, active-control, LTG monotherapy trial, dose and plasma concentration data for LTG, carbamazepine (CBZ) or phenytoin (PHT) were obtained. Following the attainment of a LTG target dose of 500 mg/day, CBZ or PHT were withdrawn in weekly 20% decrements. Following

inducer withdrawal, LTG was then continued as monotherapy for an addnl. 12 wk. Plasma concns. and daily doses of LTG, CBZ, or PHT were obtained at regularly scheduled study visits during inducer withdrawal and during LTG monotherapy. Pharmacokinetic anal. of the plasma concentration data was done to determine the time-course and effect of inducer plasma concentration on LTG oral clearance (Clo), where LTG Clo was estimated as the dose/concentration ratio. Results: Of the 156 patients enrolled in this trial, 76 were assigned to LTG arm, 43 completed the withdrawal to monotherapy phase with 28 successfully completing the study. In a subset anal. of completers, LTG Clo determined prior to withdrawal of the inducers was significantly greater in patients (n=28) on LTG+PHT (160% increase) than in those (n=48) receiving LTG+CBZ (62% increase): 1.77±0.77 vs. 1.06±0.41 mL/min/kg, resp., p=0.017. The significant reduction in LTG Clo occurred only when CBZ plasma concns. reached approx. 2 μg/mL or PHT plasma concns. reached zero. Conclusions: Mean LTG plasma concns. will approx. double following the withdrawal PHT; however increases of only 60% may occur following the withdrawal of CBZ. Importantly, these data suggest that LTG concns. would not be expected to increase until the concomitant inducer is almost completely removed.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:303722 CAPLUS
DN 137:303961
TI The benefits of reversed phases with extended polar selectivity in analyzing wide-polarity-range samples
AU Chappell, Ian
CS Alltech Associates, Applied Science Ltd, Carnforth, UK
SO LC-GC Europe (2002), 15(3), 156,158,160,162,164
CODEN: LCGCB4
PB Advanstar Communications, Inc.
DT Journal
LA English
AB Reversed phases with extended polar selectivity offer alternative selectivity to current base-deactivated reversed-phase media by allowing residual silanols to play a major role in the retention process. These phases also show reduced hydrophobic retention, which can be helpful with samples that contain both polar and nonpolar species. This article describes the use of phases with extended polar selectivity to reduce anal. time for wide-polarity-range samples, including the insecticide pirimicarb, simulated carboxylic acid degradants and phthalate esters.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 37 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:81026 CAPLUS
DN 136:303274
TI The benefits of reversed phases with extended polar selectivity in analyzing wide-polarity-range samples
AU Chappell, I.
CS Alltech Associates, Applied Science Ltd., Camforth, Lancashire, LA5 9XP, UK
SO LCGC North America (2002), 20(1), 62, 64, 66-70
CODEN: LNACBH; ISSN: 1527-5949
PB Advanstar Communications, Inc.
DT Journal
LA English
AB Reversed phases with extended polar selectivity offer alternative

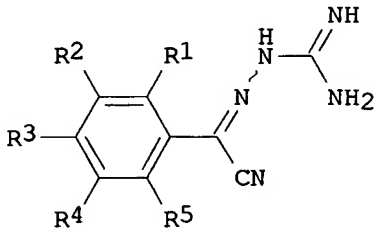
selectivity to current base-deactivated reversed-phase media by allowing residual silanols to play a major role in the retention process. These phases also show reduced hydrophobic retention, which can be helpful with samples that contain both polar and nonpolar species. This article describes the use of phases with extended polar selectivity to reduce anal. time for wide-polarity-range samples, including the insecticide pirimicarb, simulated carboxylic acid degradants, and phthalate esters.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

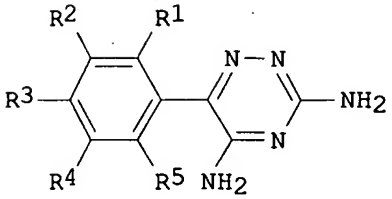
L5 ANSWER 38 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:631908 CAPLUS
DN 135:195578
TI Process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines
IN Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph
PA Chemagis Ltd., Israel
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1127873	A2	20010829	EP 2001-103660	20010223
	EP 1127873	A3	20030507		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	IL 134730	A1	20031031	IL 2000-134730	20000225
	CA 2337280	AA	20010825	CA 2001-2337280	20010215
	US 2001025118	A1	20010927	US 2001-789634	20010222
	US 6329521	B2	20011211		
PRAI	IL 2000-134730	A	20000225		

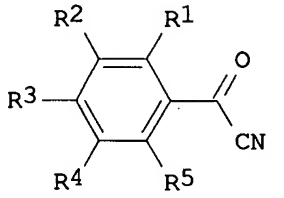
OS CASREACT 135:195578; MARPAT 135:195578
GI



I



II



III

AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as

intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were prepared by reacting the benzoyl cyanides III with aminoguanidine bicarbonate in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in PrOH to give 2,3-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L5 ANSWER 39 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:333965 CAPLUS
DN 135:251812
TI Effects of extracellular pH on the interaction of sipatrigine and lamotrigine with high-voltage-activated (HVA) calcium channels in dissociated neurones of rat cortex
AU Hainsworth, A. H.; Spadoni, F.; Lavaroni, F.; Bernardi, Giorgio; Stefani, A.
CS Section of Pharmacology, School of Pharmacy, De Montfort University, Leicester, LE1 9BH, UK
SO Neuropharmacology (2001), 40(6), 784-791
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier Science Ltd.
DT Journal
LA English
AB Acidic extracellular pH reduced high-voltage-activated (HVA) currents in freshly isolated cortical pyramidal neurons of adult rats, shifting activation to more pos. voltages (V1/2=-18 mV at pH 7.4, -11 mV at pH 6.4). Sipatrigine inhibited HVA currents, with decreasing potency at acidic pH (IC50 8 μM at pH 7.4, 19 μM at pH 6.4) but the degree of maximal inhibition was >80% in all cases (pH 6.4-8.0). Sipatrigine has two basic groups (pKA values 4.2, 7.7) and at pH 7.4 is 68% in monovalent cationic form and 32% uncharged. From simple binding theory, the pH dependence of sipatrigine inhibition indicates a protonated group with pKA 6.6. Sipatrigine (50 μM) shifted the voltage dependence of channel activation at pH 7.4 (-7.6 mV shift) but not at pH 6.4. Lamotrigine has one basic site (pKA 5.5) and inhibited 34% of the HVA current, with similar potency over the pH range 6.4-7.4 (IC50 7.5-9 μM). These data suggest that the sipatrigine binding site on HVA calcium channels binds both cationic and neutral forms of sipatrigine, interacts with a group with pKA=6.6 and with the channel activation process, and differs from that for lamotrigine.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 40 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:314796 CAPLUS
DN 135:220641
TI Retention-property relationships of anticonvulsant drugs by biopartitioning micellar chromatography
AU Martinez-Pla, J. J.; Sagrado, S.; Villanueva-Camanas, R. M.; Medina-Hernandez, M. J.
CS Facultad de Farmacia, Departamento de Quimica Analitica, Universidad de Valencia, Burjassot, Valencia, 46100, Spain
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 757(1), 89-99
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
AB Epilepsy may be considered as a group of disorders with only one thing in common: the fact that recurrent anomalous electrochem. phenomena appear in

the central nervous system. Different classes of drugs are included under the generic term of anticonvulsant drugs. All of them work by decreasing discharge propagation in different ways. Biopartitioning micellar chromatog. (BMC) is a mode of reversed-phase liquid chromatog., which can be used as an in vitro system to model the biopartitioning process of drugs when there are no active processes. In this paper, relationships between the BMC retention data of anticonvulsant drugs, their pharmacokinetics (oral absorption, protein binding, volume of distribution, clearance, and renal elimination) and their therapeutic parameters (therapeutic, toxic and comatose-fatal concentration, and LD50) are studied and the predictive ability of models is evaluated.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:181907 CAPLUS
DN 135:70536
TI Biopartitioning micellar chromatography: an in vitro technique for predicting human drug absorption
AU Molero-Monfort, M.; Escuder-Gilabert, L.; Villanueva-Camanas, R. M.; Sagrado, S.; Medina-Hernandez, M. J.
CS Departamento de Quimica Analitica, Universidad de Valencia, Burjassot, Valencia, E-46100, Spain
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 753(2), 225-236
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
AB The main oral drug absorption barriers are fluid cell membranes and generally drugs are absorbed by a passive diffusion mechanism. Biopartitioning micellar chromatog. (BMC) is a mode of micellar liquid chromatog. that uses micellar mobile phases of Brij35 under adequate exptl. conditions and can be useful to mimic the drug partitioning process in biol. systems. In this paper the usefulness of BMC for predicting oral drug absorption in humans is demonstrated. A hyperbolic model has been obtained using the retention data of a heterogeneous set of 74 compds., which shows predictive ability for drugs absorbed by passive diffusion. The model obtained in BMC is compared with those obtained using the well-known systems (Caco-2 and TC-7) that use intestinal epithelium cell lines. The use of BMC is simple, reproducible and can provide key information about the transport properties of new compds. during the drug discovery process.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:850169 CAPLUS
DN 135:40214
TI Idiosyncratic reactions: new methods of identifying high-risk patients
AU Glauser, Tracy A.
CS Children's Comprehensive Epilepsy Program, Department of Neurology, Children's Hospital Medical Center, Cincinnati, OH, 45229-3039, USA
SO Epilepsia (2000), 41(Suppl. 8), S16-S29
CODEN: EPILAK; ISSN: 0013-9580
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
AB A review with 79 refs. This article describes the mechanisms of idiosyncratic drug reactions (IDRs) and provides an anal. of potential methods for identifying patients at high risk for antiepileptic

idiosyncratic drug reactions. IDRs may be caused by toxic metabolites, either directly or indirectly (by way of an immunol. response or a free radical-mediated process). Four methods to potentially identify patients at high risk for AED IDRs are discussed: development of an "at-risk" clin. profile for a particular AED; identification of biomarkers that measure the formation of a toxic metabolite by a previously unrecognized bioactivation pathway for a particular AED; identification of biomarkers indicating deficient detoxification abilities [e.g., deficient free radical scavenging enzyme activities or low calculated oxidative protection (COP) ratios 1 and 2]; and identification of at-risk genetic markers. Clin. profiles for patients receiving valproic acid (VPA), felbamate (FBM), and lamotrigine (LTG) and who are at risk for development of AED IDRs are presented. Patients with VPA IDRs have deficient erythrocyte glutathione peroxidase activity, low plasma selenium concns., low COP1 ratios, and low COP2 ratios compared with age-matched controls. Patients with FBM-associated aplastic anemia have deficient erythrocyte glutathione peroxidase, superoxide dismutase (SOD), and glutathione reductase activities compared with age-matched controls. Use of at-risk clin. profiles (for VPA, FBM, and LTG) and measurement of erythrocyte glutathione peroxidase activity, erythrocyte SOD activity, and calcn. of COP1 and COP2 ratios (for VPA and FBM) are inexpensive, simple methods of identifying high-risk patients for IDRs. Research is needed to further characterize the mechanism of IDRs, to investigate the clin. utility of free radical-scavenging enzyme activity measurement and calcn. of COP ratios for other AED IDRs, and to develop addnl. methods of identifying patients at high risk for AED IDRs.

RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:421116 CAPLUS
DN 133:60362
TI An improved process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
IN Vyas, Sharad Kumar
PA India
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IN 183150	A	19990925	IN 1998-CA2171	19981214
	CA 2334937	AA	20000622	CA 1999-2334937	19991207
	CA 2334937	C	20040921		
	AU 2000012924	A5	20000703	AU 2000-12924	19991207
	EP 1140872	A1	20011010	EP 1999-956293	19991207
	EP 1140872	B1	20030917		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 250041	E	20031015	AT 1999-956293	19991207

	RU 2231526	C2	20040627	RU 2001-115698	19991207
PRAI	IN 1998-CA2171	A	19981214		
	WO 1999-IB1955	W	19991207		

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) (I) useful as antiepileptic drug (no data) is prepared in a 3 step process. Thus, 2,3-dichlorobenzoylchloride was treated with cuprous cyanide in presence of acetonitrile and a solvent to produce 2,3-dichlorobenzoyl cyanide, further with aminoguanidine and cyclized to produce I.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 44 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:323201 CAPLUS
DN 133:99031
TI Toward minimalistic modeling of oral drug absorption1
AU Oprea, T. I.; Gottfries, J.
CS Medicinal Chemistry, AstraZeneca R&D Molndal, Moelndal, S-43183, Swed.
SO Journal of Molecular Graphics & Modelling (2000), Volume Date 1999, 17(5/6), 261-274
CODEN: JMGMFI; ISSN: 1093-3263
PB Elsevier Science Inc.
DT Journal
LA English

AB Poor intestinal permeability of drugs constitutes a major bottleneck in the successful development of candidate drugs. Fast computational tools to help in designing compds. with increased probability of oral absorption are required, since both medicinal and combinatorial chemists are under pressure to consider increasing nos. of virtual and existing compds. The QSAR paradigm for drug absorption is expressed as a function of mol. size, hydrogen-bonding capacity, and lipophilicity. A nonlinear PLS model that can be achieved with minimal computational efforts is described. The QSAR model correlates human intestinal absorption (%HIA) data, and apparent Caco-2 cell permeability data, to parameters calculated from mol. structures. Two properties were found to be relevant for absorption predictions, namely H-bonding capacity, and hydrophobic transferability. The parsimony principle was applied in several aspects: single conformers were used to compute mol. surface areas; the definitions of "polar" and "nonpolar" surfaces were done in a simplistic fashion; simple and fast 2D descriptors were used to estimate other properties; the 1 PLS component model was selected. These choices result in a minimalistic model for oral absorption. The use of both %HIA and Caco-2 permeability data was found to stabilize and improve the model. This QSAR model can serve as a simple, quant. extension of the "rule of five" scheme, in a manner that can prove beneficial to the drug discovery process.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 45 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:17473 CAPLUS
DN 132:160834
TI Inhibition of Na+ current by diphenhydramine and other diphenyl compounds: molecular determinants of selective binding to the inactivated channels
AU Kuo, Chung-Chin; Huang, Ron-Chi; Lou, Bih-Show
CS Department of Physiology, National Taiwan University College of Medicine, and Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan
SO Molecular Pharmacology (2000), 57(1), 135-143
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English

AB Diphenhydramine is an H1 histamine receptor antagonist, yet it also has a clin. useful local anesthetic effect. We found that diphenhydramine inhibits the neuronal Na+ current, and the inhibition is stronger with more pos. holding potentials. The dissociation constant between diphenhydramine and the inactivated Na+ channel is .apprx. 10 μM, whereas the dissociation constant between diphenhydramine and the resting channel is more than 300 μM. The local anesthetic effect of diphenhydramine thus is ascribable to inhibition of Na+ current by selective binding of the drug to the inactivated channels. Most interestingly, many other compds., such as the anti-inflammatory drug diclofenac, the anticonvulsant drug phenytoin, the antidepressant drug imipramine, and the anticholinergic drug benztropine, have similar effects on neuronal Na+ current. There is no apparent common motif in the chemical structure of these compds., except that they all contain two Ph groups. Mol. modeling further shows that the two benzene rings in all these drugs have very similar spatial orientations (stem bond angle, .apprx.110 degrees; center-center distance, .apprx.5 Å). In contrast, the two Ph groups in phenylbutazone, a drug that has only a slight effect on Na+ current, are oriented in quite a different way. These findings strongly suggest that the two Ph groups are the key ligands interacting with the channel. Because the binding counterpart of a benzene ring usually is also a benzene ring, some aromatic side chain groups of the Na+ channel presumably are realigned during the gating process to make the very different affinity to the aforementioned drugs between the inactivated and the resting channels.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 46 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:795469 CAPLUS
DN 132:26963
TI Preparation of 1,2,4-triazine derivative, and its use as reference marker for testing purity and stability of lamotrigine
IN Edmeades, Lorraine Mary; Griffith-Skinner, Nigel Arthur; Hill, Derek Anthony; Hill, Graham Thornton; Packham, Terrence William
PA The Wellcome Foundation Limited, UK
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 963980	A2	19991215	EP 1999-200695	19990310
	EP 963980	A3	20000531		
	EP 963980	B1	20020605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	SG 85628	A1	20020115	SG 1999-1252	19990225
	MX 9902202	A	20000831	MX 1999-2202	19990305
	KR 2000005611	A	20000125	KR 1999-7632	19990309
	HR 990074	A1	20001031	HR 1999-990074	19990309
	ZA 9901951	A	19990816	ZA 1999-1951	19990310
	JP 2989189	B2	19991213	JP 1999-63792	19990310
	JP 2000009714	A2	20000114		
	NO 9901151	A	19991213	NO 1999-1151	19990310
	CN 1238454	A	19991215	CN 1999-103445	19990310
	AU 9920319	A1	20000106	AU 1999-20319	19990310
	TR 9900520	A2	20000121	TR 1999-520	19990310
	BR 9900984	A	20000502	BR 1999-984	19990310
	NZ 334590	A	20000728	NZ 1999-334590	19990310

	CA 2265194	C	20001010	CA 1999-2265194	19990310
	US 6333198	B1	20011225	US 1999-265670	19990310
	EP 1170588	A1	20020109	EP 2001-203376	19990310
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 218552	E	20020615	AT 1999-200695	19990310
	PT 963980	T	20021031	PT 1999-200695	19990310
	ES 2178342	T3	20021216	ES 1999-200695	19990310
	CN 1306210	A	20010801	CN 2000-122208	20000725
	US 2002055177	A1	20020509	US 2001-940422	20010829
	NO 2003002753	A	19991213	NO 2003-2753	20030617
PRAI	GB 1998-12413	A	19980610		
	EP 1999-200695	A3	19990310		
	US 1999-265670	A3	19990310		

AB A method of testing the purity or stability to degradation of a sample of lamotrigine or a pharmaceutical dosage form comprising lamotrigine consists of assaying the sample for the presence of a compound selected from 3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-5-(4H)-one and N-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-3-yl]-2,3-dichlorobenzamide (I). A process for producing compound I, is also disclosed. Lamotrigine was treated with 2,3-dichlorobenzoyl chloride to give I. TLC-densitometry was used to determine I in lamotrigine tablets.

L5 ANSWER 47 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:215943 CAPLUS
DN 131:40039
TI Effect of sodium nitroprusside and lamotrigine on aspartate release from mouse brain cortex sections
AU Afanas'ev, I. I.; Kudrin, V. S.; Varga, V.; Saransaari, R.; Oiya, S.; Raevskii, K. S.
CS Laboratosy of Neurochemical Pharmacology, Institute of Pharmacology, Russian Academy of Medical Sciences, Moscow, 125315, Russia
SO Eksperimental'naya i Klinicheskaya Farmakologiya (1998), 61(6), 9-12
CODEN: EKFAE9; ISSN: 0869-2092
PB Izdatel'stvo Folium
DT Journal
LA Russian
AB The effects of nitrous oxide and the antiepileptic agent lamotrigine on nonstimulated and K+- and veratridine-stimulated release of D-[3H]aspartate from brain cortex sections of mice were studied. Sodium nitroprusside (0.1 mM) intensified nonstimulated (by 38 - 52%) and K+-stimulated (by 86%) release of labeled D-aspartate. Lamotridgin (0.1 mM) inhibited nonstimulated and veratridine-stimulated release of the labeled D-aspartate (by 50 and 70%, resp.). Sodium nitroprusside completely reversed the inhibiting affect of lamotrigine on spontaneous and veratridine-stimulated release of D-aspartate. It is suggested that NMDA-subtype presynaptic receptors contribute to the regulation of D-aspartate release and the process is modulated by nitrous oxide.

L5 ANSWER 48 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:688698 CAPLUS
DN 130:133985
TI Effect of lamotrigine on cerebral edema following traumatic brain injury in rats
AU Cheng, Yuan; Chen, Furen; Wu, Ying; Zhang, Xiaoping
CS Department of Neurosurgery, Chongqing Medical University 2nd Clinical College, Chungking, 400042, Peop. Rep. China
SO Zhonghua Chuangshang Zazhi (1998), 14(4), 209-211
CODEN: ZCZAFD; ISSN: 1001-8050
PB Zhonghua Chuangshang Zazhi Bianjibu

DT Journal
LA Chinese
AB Rat impacted brain injury models were used to conduct the study. Water content measured by drying-wet brain weight was increased, the injured brain tissue glutamine were increased after the injury; and the water and glutamine exhibited a self diffusion process. In the lamotrigine treated animals, the brain tissue water and glutamine contents increased after injury were significantly reduced, P< 0.01, 0.05. The results suggest that the lamotrigine is effective in reducing the cerebral edema after acute brain injury through the inhibition of releasing glutamine from the neuron.

L5 ANSWER 49 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:681065 CAPLUS
DN 130:47407
TI A common anticonvulsant binding site for phenytoin, carbamazepine, and lamotrigine in neuronal Na+ channels
AU Kuo, Chung-Chin
CS Department of Physiology, National Taiwan University College of Medicine, and Department of Neurology, National Taiwan University Hospital, Taichung, Taiwan
SO Molecular Pharmacology (1998), 54(4), 712-721
CODEN: MOPMA3; ISSN: 0026-895X
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Phenytoin, carbamazepine, and lamotrigine are anticonvulsants frequently prescribed in seizure clinics. These drugs all show voltage-dependent inhibition of Na+ currents, which has been implicated as the major mechanism underlying the antiepileptic effect. This study examined the inhibition of Na+ currents by mixts. of different anticonvulsants. Quant. anal. of the shift of steady state inactivation curve in the presence of multiple drugs argues that one channel can be occupied by only one drug mol. Moreover, the recovery from inhibition by a mixture of two drugs (a fast-unbinding drug plus a slow-unbinding drug) is faster, or at least not slower, than the recovery from inhibition by the slow-unbinding drug alone. Such kinetic characteristics further strengthen the argument that binding of one anticonvulsant to the Na+ channel precludes binding of the other. It is also found that these anticonvulsants are effective inhibitors of Na+ currents only when applied externally, not internally. Altogether these findings suggest that phenytoin, carbamazepine, and lamotrigine bind to a common receptor located on the extracellular side of the Na+ channel. Because these anticonvulsants all have much higher affinity to the inactivated state than to the resting state of the Na+ channel, the anticonvulsant receptor probably does not exist in the resting state. Thus, there may be correlative conformational changes for the making of the receptor on the extracellular side of the channel during the gating process.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 50 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:482531 CAPLUS
DN 129:213229
TI Nuclear relaxation analysis of the xenobiotic-receptor (DNA or plasma protein) recognition process
AU Bonechi, C.; Donati, A.; Loiselle, S.; Martini, S.; Picchi, M. P.; Rossi, C.
CS Dept. of Chemical and Biosystem Sciences, University of Siena, Siena, 53100, Italy
SO Spectroscopy Letters (1998), 31(5), 1039-1051

CODEN: SPLEBX; ISSN: 0038-7010
PB Marcel Dekker, Inc.
DT Journal
LA English
AB The study of interactions of xenobiotics with macromol. receptors is very important for understanding the chemical behavior of xenobiotic compds. in biol. organisms. The xenobiotic mols. are able to affect the natural activities of biol. receptors such as DNA or plasma proteins. In fact, the modification of the conformation of DNA or plasma protein, induced by interaction with xenobiotic mols., can determine profound alterations of the normal biochem. activity. In this study a method based on proton NMR selective and non-selective spin-lattice relaxation rate measurements and their dependence on temperature is used for analyzing the ability of ligand to interact with receptor. The NMR parameters are a weighted average between the free and xenobiotic-bound environments.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 51 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:36233 CAPLUS
DN 126:54374
TI The new antiepileptic drugs and women: efficacy, reproductive health, pregnancy, and fetal outcome
AU Morrell, Martha J.
CS Stanford Comprehensive Epilepsy Center, Stanford University Medical School, Stanford, CA, USA
SO Epilepsia (1996), 37(Suppl. 6), S34-S44
CODEN: EPILAK; ISSN: 0013-9580
PB Lippincott-Raven
DT Journal; General Review
LA English
AB A review with .apprx.107 refs. As new antiepileptic drugs (AEDs) become available, physicians will define their appropriate use in particular patient populations. For women, the issues include gender-specific efficacy and tolerability, including the impact of the AED on reproductive health. Women with epilepsy who are treated with established AEDs appear to be at risk for compromised bone health, for disturbances in fertility, menstrual cyclicity, ovulatory function, and sexuality and, with some AEDs, for failure of hormonal contraception. Finally, pregnancy outcome may be adversely affected by the established AEDs, all of which are human teratogens. Felbamate (FBM), gabapentin (GBP), lamotrigine (LTG), oxcarbazepine (OCBZ), tiagabine (TGB), topiramate (TPM), and vigabatrin (VGB) were reviewed. The preclin. development process had not addressed all the issues of concern to women. Although gender-specific efficacy is routinely evaluated, impact on reproductive health is not. FBM, GBP, LTG, TGB, TPM, and VGB have similar efficacy in women and men. It is not known whether the new AEDs will affect bone health, fertility, the menstrual cycle, and sexuality. FBM, GBP, LTG, TGB, and probably VGB do not interfere with hormonal contraception. Whether these new AEDs are good choices for the pregnant woman with epilepsy awaits further experience in human pregnancy. However, animal reproductive toxicol. studies appear promising. The limited number of human pregnancy exposures do not, thus far, signal a significant number or particular type of adverse outcomes. However, only with improved postmarketing surveillance can essential information about teratogenic effects be acquired in an acceptably short time.

L5 ANSWER 52 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:196405 CAPLUS
DN 124:307192
TI Neuroprotective strategies for treatment of lesions produced by

mitochondrial toxins: implications for neurodegenerative diseases
AU Schulz, J. B.; Matthews, R. T.; Henshaw, D. R.; Beal, M. F.
CS Neurochemistry Lab., Harvard Med. Sch., Boston, MA, 02114, USA
SO Neuroscience (Oxford) (1996), 71(4), 1043-8
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier
DT Journal
LA English
AB Neuronal death in neurodegenerative diseases may involve energy impairment leading to secondary excitotoxicity, and free radical generation. Potential therapies for the treatment of neurodegenerative diseases therefore include glutamate release blockers, excitatory amino acid receptor antagonists, agents that improve mitochondrial function, and free radical scavengers. In the present study we examined whether these strategies either alone or in combination had neuroprotective effects against striatal lesions produced by mitochondrial toxins. The glutamate release blockers lamotrigine and BW1003C87 significantly attenuated lesions produced by intrastriatal administration of 1-methyl-4-phenylpyridinium. Lamotrigine significantly attenuated lesions produced by systemic administration of 3-nitropropionic acid. Memantine, an N-methyl-D-aspartate antagonist, protected against-malonate induced striatal lesions. We previously found that coenzyme Q10 and nicotinamide, and the free radical spin trap n-tert-butyl-α-(2-sulfophenyl)-nitrone (S-PBN) dose-dependently protect against lesions produced by intrastriatal injection of malonate. In the present study we found that the combination of MK-801 (dizocipiline) with coenzyme Q10 exerted additive neuroprotective effects against malonate. Lamotrigine with coenzyme Q10 was more effective than coenzyme Q10 alone. The combination of nicotinamide with S-PBN was more effective than nicotinamide alone. These results provide further evidence that glutamate release inhibitors and N-acetyl-D-aspartate antagonists can protect against secondary excitotoxic lesions in vivo. Furthermore, they show that combinations of agents which act at sequential steps in the neurodegenerative process can produce additive neuroprotective effects. These findings suggest that combinations of therapies to improve mitochondrial function, to block excitotoxicity and to scavenge free radicals may be useful in treating neurodegenerative diseases.

L5 ANSWER 53 OF 53 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:178310 CAPLUS
DN 114:178310
TI The effect of lamotrigine upon development of cortical kindled seizures in the rat
AU O'Donnell, R. A.; Miller, A. A.
CS Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SO Neuropharmacology (1991), 30(3), 253-8
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB The effect of lamotrigine, a novel potential antiepileptic drug, upon the development of kindled cortical seizures was investigated in rats. Although lamotrigine, at all doses tested, failed to block or reduce the rate of development of kindling, it did have a profound effect upon the production of both non-kindled and kindled responses. All doses (3, 6, 12, and 18 mg/kg) produced a significant increase in the number of nil responses (where stimulation failed to evoke a behavioral clonus or afterdischarge) and a decrease in non-kindled responses. Doses of 12 and 18 mg/kg also significantly reduced the number of kindled responses and the duration of the kindled seizure. It is suggested that these effects of lamotrigine result from its ability to inhibit the release of glutamate, an excitatory amino acid which has been implicated in the production of kindled seizures. In

contrast to previous studies on the development of kindling, it was found that in the groups which received either 12 or 18 mg/kg lamotrigine, it was possible to produce kindling without evoking any nonkindled afterdischarge. This finding is discussed in the light of the current theories surrounding the kindling process. This study suggests that lamotrigine, as well as possibly being of value in the treatment of complex partial and generalized (tonic-clonic) seizures, may also be of value in the treatment of elementary (simple) partial seizures.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	159.68	165.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-39.75	-39.75

STN INTERNATIONAL LOGOFF AT 09:08:42 ON 22 SEP 2006

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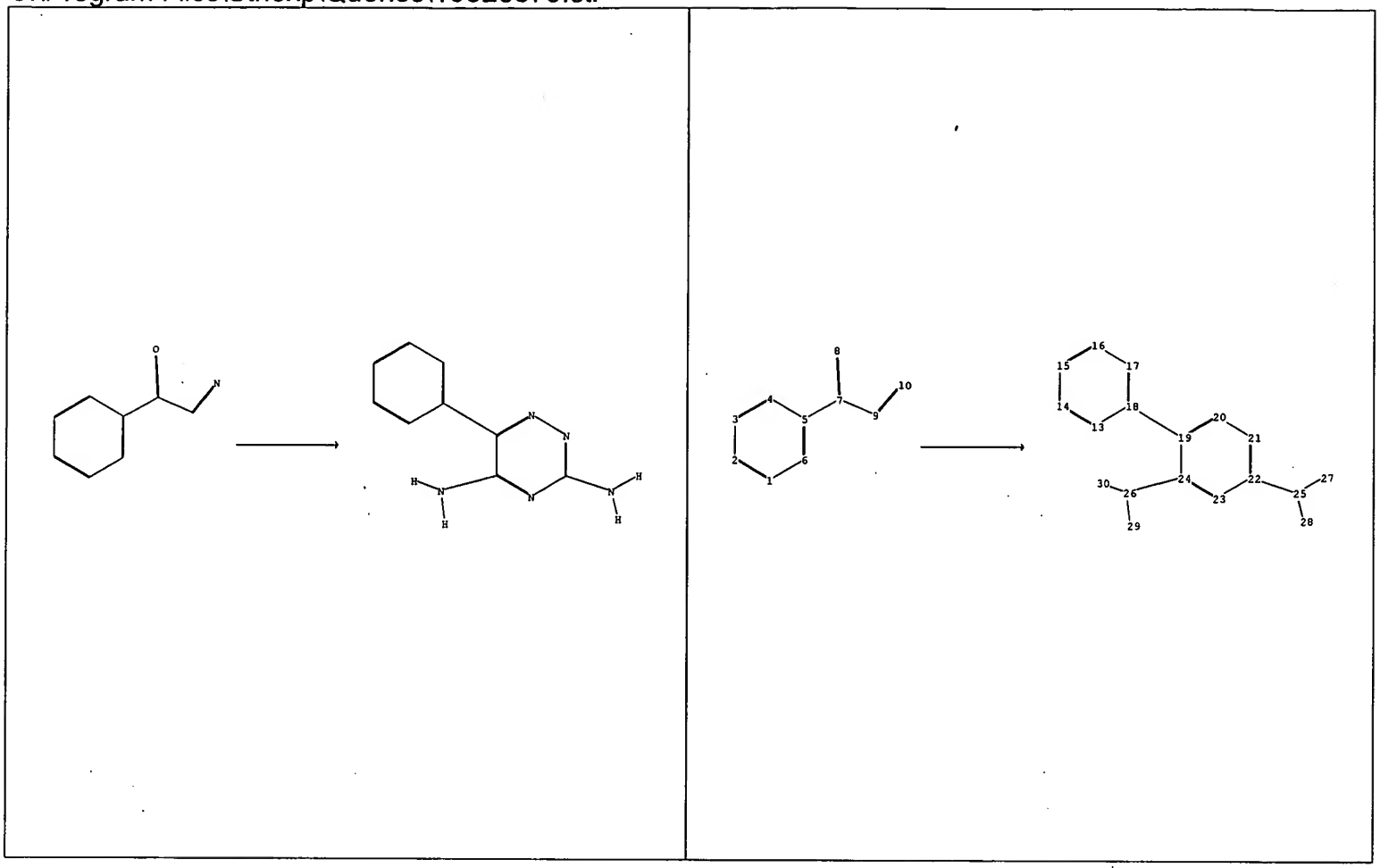

chain nodes :
7 8 9 10 25 26 27 28 29 30
ring nodes :
1 2 3 4 5 6 13 14 15 16 17 18 19 20 21 22 23 24
chain bonds :
5-7 7-8 7-9 9-10 18-19 22-25 24-26 25-27 25-28 26-29 26-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18 19-20 19-24 20-21 21-22 22-23 23-24
exact/norm bonds :
7-8 9-10 22-25 24-26
exact bonds :
5-7 7-9 18-19 25-27 25-28 26-29 26-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18 19-20 19-24 20-21 21-22 22-23 23-24

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS
fragments assigned product role:
containing 13
fragments assigned reactant/reagent role: